102

CYTOMEGALOVIRUS (CMV) INFECTION IN ALLOGENEIC NON-MYELOABLATIVE STEM CELL TRANSPLANTATION RECIPIENTS

Chandrasekar, P.[1], King, R.[2], Dansey, R.[2], Akhtar, A.[2], Mellon-Reppen, S.[2], Alangaden, G.[1] 1. Infectious Disease Division, Detroit, MI; 2. Bone Marrow Transplant, Detroit, MI.

Background: Non-myeloablative technique of allogeneic stem cell transplantation is recent and increasingly popular; data regarding CMV infection are limited in such transplant recipients. **Methods:** We examined our data on patients undergoing non-myeloablative transplantation (NMT) during Sept 2000-Dec 2002. **Results:** Thirty-one patients (men 16, mean age 54; women 15, mean age 47) underwent non-myeloablative transplantation (NMT) during Sept 2000-Dec 2002 (Number of patients: 3-2000; 16-2001; 12-2002). Major underlying diseases were renal cell carcinoma (11), myeloma (5), Non-Hodgkin's lymphoma (5) and breast cancer (3). Of 31 patients, 10 received matched unrelated donor stem cells. Preparative regimens were Fludarabine with cyclophosphamide (19 patients) or fludarabine with total body irradiation (12 patients). Most (29/31) received peripheral blood stem cells. Mean duration of neutropenia was 6.6 days (range 0-16). Fifteen of 31 patients were CMV seropositive. None received prophylaxis against CMV; CMV antigen (pp65) test was routinely done once weekly. CMV antigenemia occurred in 12 patients (with viremia in 3), 9 of whom were seropositive and 3 seronegative, after a mean duration of 56 days (range 24-165) from transplant. Antigenemia after 100 days occurred in only 1 patient. Four of 12 patients with antigenemia had received stem cells form unrelated donors. None developed CMV disease. Of the total 31 patients transplanted, 19 died. CMV antigenemia was of low level in most patients with prompt response to IV ganciclovir. **Conclusions:** Our preliminary data demonstrate that CMV infection is common in NMT recipients; routine surveillance and pre-emptive therapy with ganciclovir are effective in preventing CMV disease.

103

ANTI-DONOR ISOAGGLUTININ REDUCTION AND PURE RED CELL APLASIA AFTER MAJOR ABO-INCOMPATIBLE HSCT

Stussi, G.[1], Bucheli, E.[1], Passweg, J.R.[2], Halter, J.[1], Schanz, U.[1], Gmuer, J.[1], Gratwoh, L.A.[2], Seebach, J.D.[1] 1. University Hospital, Zurich, Switzerland; 2. University Hospital, Basel, Switzerland.

Posttransplant pure red cell aplasia (PRCA) occurs after major or bidirectional ABO-incompatible HSCT and presumably is caused by the persistence or a secondary rise of anti-donor host B cells. However, it is not known, whether the incidence of PRCA depends on the level and/or reduction of anti-donor isoagglutinins prior to HSCT. We performed a retrospective two-center analysis of 153 consecutive patients receiving major (n = 123) or bidirectional (n = 46) ABO incompatible, allogeneic HSCT between 1980 and 2002. Posttransplant PRCA was defined as reticulocyte count of less than 1% for more than 100 days along and a lack of RBC precursors in a bone marrow specimen. In one center, isoagglutinins of the recipient were removed by plasma exchange and/or *in-vivo* absorption (IVA) with pretransplant transfusion of donor-type RBC. Consequently, these patients received exclusively donor-type RBC after HSCT. The other center depleted donor stem cells from RBC and transfused recipient- or O-type RBC as long as anti-donor isoagglutinins were present. Overall, 12 patients developed PRCA after HSCT (12/153, 7.8%). All received HSCT from a major ABO-incompatible donor. The mean RBC take was delayed to 224 d in patients with PRCA (range 143-382 d) compared to 24 d and the requirement for RBC transfusions was increased (36 vs. 12, $p < 0.001$). RBC engraftment was associated with a simultaneous decrease of anti-donor isoagglutinins (11/12). Remarkably, 9/12 patients with PRCA were transplanted in the center where isoagglutinin titers were not reduced prior to HSCT. In this center, 9/46 patients (20%) developed PRCA, whereas only 3 cases occurred in the other center (3/107, 3%, $p < 0.001$). Patients with PRCA had higher pretransplant isoagglutinin titers (median 1:64 vs. 1:16, $p < 0.001$). Pretransplant IVA resulted in hemolysis, but had no serious side effects. The time to RBC engraftment was also delayed after exclusion of patients with PRCA indicating a general negative effect of anti-donor isoagglutinins on erythropoiesis ($p = 0.005$). Beside pretransplant IVA, peripheral stem cell source was the only significant variable in multivariate analysis positively associated with RBC engraftment. In summary, PRCA after HSCT depends on the levels and/or reduction of pretransplant anti-donor isoagglutinins. IVA of these antibodies by transfusions of incompatible RBC seems to be a feasible, safe, and cost-effective method to prevent the occurrence of PRCA.

104

PARTIAL T CELL DEPLETION FOR UNRELATED DONOR BMT FOR CHILDREN WITH SEVERE APLASTIC ANEMIA (SAA): ENGRAFTMENT WITH MINIMAL GVHD

Bunin, N., Leahey, A., Grupp, S., Pierson, G., Monos, D. Children's Hospital of Philadelphia, Philadelphia, PA.

Unrelated donor BMT for SAA is reserved for patients who lack an HLA identical sibling, and fail medical therapy. However, increased graft rejection is a potential problem in these heavily transfused patients (pts), and the risk of severe GVHD is also increased with unrelated donors. Improved techniques in HLA typing to ensure molecular matching may decrease the risk of GVHD, but may limit donor availability. Partial T cell depletion may decrease the risk of severe GVHD, while still maintaining sufficient donor T lymphocytes to ensure engraftment. We report on 12 patients with SAA who underwent unrelated donor BMT. Pts had failed medical therapy with ATG, steroids and cyclosporine (CSA) (9) or relapsed following initial responses (3). Median age was 6 yrs (1-20), and there were 5 males, 7 females. Median time from diagnosis of SAA to BMT was 466 days(155-1084). Donors were serology class I (A, B) and DRB1 matched for 4 pts, mismatched at the A locus for 3 pts, at B locus for 3 pts, and at DR for 2 pts. Conditioning included Ara-C 12 g/m^2, cyclophosphamide (CPM) 90 mg/kg and total body irradiation 12-13.2 Gy for 4 pts, and thiotepa 10 mg/kg, CPM 120 mg/kg and TBI 12 Gy for 8 pts. The last 7 pts received ALG 1.5 mg/kg for 3 days prior to marrow infusion. *In* vitro partial T cell depletion was T10B9 and complement (8 pts) or OKT3 and complement (4 pts). Cyclosporine was used for 3 months post BMT and then tapered. Median nucleated cell dose post T depletion was 0.8 x 10^8/kg (0.24-3.2), and median CD3+ cell dose was 1 x 10^6/kg (0.2-9.2). All patients engrafted, with a median time of 18 days to ANC > 500 (14-34), and all but one pt became platelet transfusion independent. Acute GVHD grades I-II developed in 4 pts; two developed limited cGVHD. Nine pts (75%) are alive 3-147 mos post BMT and transfusion independent. Morbidity included intractable VOD in a pt with Schwachman-Diamond syndrome, who underwent successful related donor live transplant. Three pts died at d 165, 237 and 282 from resistant CMV, renal failure, and PCP respectively. This series suggests that an aggressive immunosuppressive conditioning regimen with partial T cell depletion results in successful engraftment and minimal GVHD in pediatric patients with SAA, even with HLA mismatched donors.

105

ANTI-THYMOCYTE-GLOBULIN (ATG) IN THE NONMYELOABLATIVE CONDITIONING FOR CANINE HEMATOPOIETIC CELL TRANSPLANT (HCT)

Diaconescu, R.[1], Little, M.-T.[1], Leisenring, W.[1,2], Yunusov, M.[1], Hogan, W.[1], Sorror, M.[1], Baron, F.[1], Storb, R.[1,2] 1. Fred Hutchinson Cancer Research Center, Seattle, WA; 2. University of Washington, Seattle, WA.

We tested whether pretransplant immunosuppression with canine-specific rabbit ATG (SangStat), combined with 1 Gy total body irradiation (TBI) and posttransplant mycophenolate mofetil/cyclosporine (MMF/CSP) would assure stable engraftment in our canine HCT model. First, pharmacokinetic studies were done in 4 dogs, with cumulative ATG doses of 2–5 mg/kg, subcutaneously. ATG was most effective in depleting peripheral T cells (CD4+ and CD8+), intermediate on B cells and did not deplete other blood cells. Lymph node biopsies taken after 2 mg/kg ATG showed 50% T-cell depletion. Serum levels of ATG peaked at